Complete Summary

GUIDELINE TITLE

Consultation and referral guidelines citing the evidence: how the allergist-immunologist can help.

BIBLIOGRAPHIC SOURCE(S)

American Academy of Allergy, Asthma & Immunology. Consultation and referral guidelines citing the evidence: how the allergist-immunologist can help. J Allergy Clin Immunol 2006 Feb;117(2 Suppl Consultation):S495-523. [371 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Allergies and allergic reactions, including:

- Allergic bronchopulmonary aspergillosis
- Anaphylaxis
- Asthma
- Conjunctivitis
- Cough
- Dermatitis (atopic and contact)
- Drug allergy
- Food allergy
- Hypersensitivity pneumonitis

- Insect hypersensitivity
- Occupational allergic diseases
- Primary immune deficiency
- Rhinitis, sinusitis, & rhinosinusitis
- Urticaria with or without angioedema (e.g., caused by ingestants, contactants, C1 esterase inhibitor deficiency)

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Treatment

CLINICAL SPECIALTY

Allergy and Immunology

INTENDED USERS

Allied Health Personnel
Health Care Providers
Health Plans
Patients
Physicians

GUIDELINE OBJECTIVE(S)

- To define both the expertise of the allergist-immunologist and under what circumstances they can be of added value in the treatment of patients
- To assist patients and health care professionals in determining when referral to an allergist-immunologist could be helpful

TARGET POPULATION

Adults and children with allergies or asthma

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Evaluation

1. Allergen skin testing for specific immunoglobulin E (IgE)
2. In vitro tests for specific IgE
3. History-specific IgE correlation
4. Allergy challenges (e.g., to methacholine, histamine, cold air, exercise, food ingestion, drug challenges)
5. Pulmonary function tests (e.g., spirometry, peak flow)
6. Immune competence

Nonpharmacologic Management

1. Education regarding appropriate avoidance behavior
2. Written management plan
3. Industrial hygiene survey assistance
4. Education regarding self-monitoring
5. Education regarding self-treatment

Pharmacologic and Immunologic Management

1. Inhaled and oral corticosteroids
2. Immunomodulator therapy
3. Inhalant immunotherapy
4. Venom immunotherapy
5. Desensitization therapy (e.g., to antibiotics, insulin, aspirin and other nonsteroidal anti-inflammatory drugs)

MAJOR OUTCOMES CONSIDERED

- Sensitivity/specificity of diagnostic tests
- Accuracy of diagnosis
- Direct and indirect outcomes of interventions performed by the allergist/immunologist

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Many American Academy of Allergy, Asthma and Immunology committees and individuals:

- Determined the guideline scope and clinical objectives
- Defined and conducted appropriate and comprehensive literature searches
- Sorted and evaluated the evidence

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

- Ia. Meta-analysis of randomized controlled trials
- Ib. Randomized controlled trial
- II. Nonrandomized, controlled intervention study
- III. Observational cohort or case-control study
- IV. Review article, expert opinion

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Recommendations were based on expert interpretation of the evidence.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Published cost analyses were reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guidelines were reviewed and approved by the American Academy of Allergy, Asthma and Immunology (AAAAI) leadership and presented to the AAAAI membership for comments before being finalized.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

This document includes specific referral guidelines for 14 categories of allergic diseases, along with the rationale for the referral, references, and the type and grade of evidence provided (Tables I to XIV). The tables are presented

alphabetically for easy navigation and do not refer to the prevalence of the individual disease. Guideline grades of evidence (Ia, Ib, II, III, IV) are defined at the end of the "Major Recommendations" field.

TABLE I. Allergic Bronchopulmonary Aspergillosis (ABPA)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with suspected or proven asthma or cystic fibrosis who have pulmonary infiltrates and peripheral blood eosinophilia	Allergen skin testing and *in vitro* tests, when correlated with history and other findings, can establish the diagnosis of ABPA (Greenberger, 2002)	IV	Diagnostic
Patients with known ABPA for management	Allergist-immunologists are specifically trained to manage this disease ("Allergy and immunology core curriculum," 1996), and outcomes of such management have been reported by allergist-immunologists (Patterson et al., 1982; Patterson et al., 1986; Patterson et al., 1987).	III, IV	Indirect outcome (ABPA management)

TABLE II. Anaphylaxis (see also "Drug allergy" [Table VII], "Food allergy" [Table VIII], and "Insect hypersensitivity" [Table X] for anaphylaxis caused by these agents)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Individuals with a severe allergic reaction (anaphylaxis) without an obvious or previously defined trigger	After a severe allergic reaction without a known cause, a trigger should be identified if at all possible. An allergist-immunologist is the most appropriate medical professional to perform this evaluation ("Allergy and immunology core curriculum," 1996), which might include skin testing, *in vitro* tests, and challenges when indicated (including with exercise, see below). Major triggers for anaphylaxis are foods and food constituents, medications and biologic agents, latex, and insect stings (Cianferoni et al., 2001; Brown, McKinnon, & Chu, 2001; Lee & Greenes, 2000; Yocum et al., 1999; Akin & Metcalfe, 2004). Future avoidance of the identified triggers should prevent	III, IV	Diagnostic Indirect outcome (trigger avoidance)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	subsequent anaphylactic episodes.		
	Management of idiopathic anaphylaxis by an allergist-immunologist is associated with a reduction in hospitalizations and emergency department visits (Wong, Dykewicz, & Patterson, 1990).	III	Direct outcome (idiopathic anaphylaxis)
Persons with anaphylaxis attributed to food	Food allergy is the most common cause of anaphylaxis outside of the hospital setting (Cianferoni et al., 2001; Brown, McKinnon, & Chu, 2001; Yocum et al., 1999). Allergist-immunologists use diagnostic modalities to confirm the trigger and use their specific training ("Allergy and immunology core curriculum," 1996) and clinical experience to educate patients regarding avoidance and immediate management to prevent potentially deadly outcomes (Bock, Munoz-Furlong, & Sampson, 2001).	III, IV	Diagnostic Indirect outcome (food avoidance, early interventions)
Exercise-induced anaphylaxis and food-dependent exercise-induced anaphylaxis	After an anaphylactic reaction that appears to have a significant relationship to exercise, it is crucial to be certain whether exercise is the cause and to determine whether a food might be involved (Sheffer et al., 1983; Casale, Keahey, & Kaliner, 1986; Romano et al., 2001; Aihara et al., 2001).	II, III	Diagnostic Indirect outcome (avoidance)
Drug-induced anaphylaxis	Allergist-immunologists use diagnostic agents to confirm the drug responsible for the reaction, if these agents are available (see "Drug allergy" [Table VII]).		Diagnostic

TABLE III, A. Asthma Diagnosis

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with respiratory symptoms suggestive of asthma but with normal PFT results (FEV_1 >80% of predicted value) and no significant reversibility (<12% and 200-mL increase in	Allergists-immunologists perform methacholine challenges, which have a high sensitivity for current asthma (Hopp, et al., 1984; Cockcroft et al., 1992).	III	Diagnostic

Referral Guideline	Rationale	Evidence Grade	Evidence Type
FEV_1)			
Exercise-induced symptoms that are atypical or do not respond well to pretreatment with albuterol, nedocromil, or cromolyn	Further objective evaluation and confirmation with pulmonary function testing (including exercise challenge) in conjunction with appropriate allergist-immunologist evaluation will define diagnosis or differential diagnosis (Holzer, Anderson, & Douglass, 2002).	III	Diagnostic
Subjects wishing to scuba dive with a history of asthma	There is a theoretic risk of increased barotraumas, as well as exercise-induced bronchospasm, in patients with asthma who scuba dive. Bronchoprovocation with exercise has been recommended to exclude asthma in scuba divers (Anderson et al., 1995).	IV	Diagnostic Indirect outcome (scuba diving avoidance)

PFT = pulmonary function test; FEV_1 = 1-second forced expiratory volume

TABLE III, B. Asthma: Environmental Diagnosis and Management

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with a history of seasonal or persistent asthma for evaluation of inhalant sensitization to confirm the diagnosis	Exposure to indoor and outdoor allergens can worsen asthma (Bjornsson et al., 1995; Marks et al., "Mite allergen", 1995; Henderson et al., 1995; Newson et al., 1997; Marks et al., 2001; Pollart et al., 1988; Subiza et al., 1994; Epton et al., 1997; Neas et al., 1996; Targonski, Persky, & Ramekrishnan, 1995; Dales et al., 2000; Vervloet et al., 1991; Kivity et al., 1993; Custovic et al., 1996; Rosenstreich et al., 1997). Allergy cannot be diagnosed on the basis of history alone (Host et al., 2003). Diagnosis is derived from correlation of clinical history and diagnostic tests (Host et al., 2003), with which allergist-immunologists are expert ("Allergy and immunology core curriculum," 1996.	III, IV	Diagnostic
Patients who need management and education concerning environmental triggers	Allergists have familiarity with the wide variety of both indoor and outdoor aeroallergen exposures that have been shown to affect asthma and respiratory function (Core	Ib, II, III, IV	Indirect outcome (avoidance)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	Curriculum Subcommittee, 1996). Allergists are specifically trained to provide education regarding appropriate avoidance measures ("Allergy and immunology core curriculum," 1996). Allergen avoidance can improve asthma (Platts-Mills et al., 1982; Dorward et al., 1988; Ehnert et al., 1992; Boner et al., 1985; Grootendorst et al., 2001; Marks et al., "The effect of changes", 1995; Carswell et al., 1996; Halken et al., 2003; Frederick et al., 1997; Shapiro et al., 1999; Cloosterman et al., 1999; Warner et al., 2000; Van der Heide et al., 1997).		
Patients with asthma who experience a worsening of symptoms after a new pet has been introduced into the home	Exposure to furred pets in allergic patients can worsen asthma symptoms (Sporik et al., 1995; Bollinger et al., 1996). Avoidance of pets in allergic patients can improve asthma symptoms (Van der Heide et al., 1999), reduce airway responsiveness (Shirai et al., 2005), and reduce the need for inhaled corticosteroids (Shirai et al., 2005).	Ib, III, IV	Diagnostic Indirect outcome (avoidance)

TABLE III, C. Asthma Treatment: Immunotherapy

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Consider referral for allergen immunotherapy for asthmatic patients if there is a clear relationship between asthma and exposure to an unavoidable aeroallergen to which specific IgE antibodies have been demonstrated and the following: • poor response to pharmacotherapy or avoidance measures • unacceptable side effects of medications • desire to avoid long-term pharmacotherapy • coexisting allergic	The efficacy of allergen immunotherapy in the treatment of allergic asthma has been demonstrated in many double-blind, placebo-controlled studies to multiple allergens (e.g., pollen, animal allergen, fungi, and dust mite) ("Allergen immunotherapy," 2003; Abramson, Puy, & Weiner, 1995; Ross, Nelson, & Feingold, "Effectiveness of specific immunotherapy in the treatment of asthma," 2000).	Ia, Ib, IV	Indirect outcome (immunotherapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
rhinitis • long duration of symptoms (perennial or major portion of the year)			
Consider referral for children with allergic rhinitis because immunotherapy can potentially prevent the development of asthma	One study suggests that allergen immunotherapy has been shown to reduce the development of asthma in children with allergic rhinitis compared with a group of children treated with medication alone (Moller et al., 2002) Immunotherapy might also prevent the development of new allergen sensitivities (Purello-D'Ambrosio et al., 2001; Des Roches et al., 1997; Pajno et al., 2001)	Ib, II, III	Indirect outcome (immunotherapy)

IgE = immunoglobulin E

TABLE III, D. Asthma Treatment: Prevention of Morbidity

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with asthma who require emergency department care for an acute episode	Allergist care reduces subsequent asthma emergency department visits (Moore et al., 1997; Vilar et al., 2000; Wu et al., 2001; Kelly et al., 2000; Zeiger et al., 1991; Westley et al., 1997; Sperber et al., 1995; Weinstein et al., 1992; Weinstein et al., 1996; Schatz et al., 2003; Schatz et al., 2005).	Ib, II, III	Direct outcome
	Allergist care reduces subsequent hospitalization (Vilar et al., 2000; Wu et al., 2001; Kelly et al., 2000; Zeiger et al., 1991; Westley et al., 1997; Sperber et al., 1995; Weinstein et al., 1992; Weinstein et al., 1996; Schatz et al., 2003; Schatz et al., 2005).	Ib, II, III	
Patients with uncontrolled asthma	Allergist care reduces asthma symptoms and improves physical functioning and asthma-related quality of life (Moore et	II, III	Direct outcome

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	al., 1997; Wu et al., 2001; Schatz et al., 2005; Vollmer et al., 1997).		
Patients with persistent asthma, particularly moderate-to-severe persistent asthma	Inhaled corticosteroid use leads to reduction in asthma symptoms, exacerbations, hospitalizations, and asthma death (Schatz et al., 2003).	Ib	Indirect outcome (controllers)
	Allergist care is more likely to lead to use of asthma controller medications (particularly inhaled corticosteroids) (Zeiger et al., 1991; Sperber et al., 1995; Schatz et al., 2003; Vollmer et al., 1997; Stempel, Carlson, & Buchner, 1997; Diette et al., 2001; Mahr & Evans, 1993).	Ib, II, III	
	Allergists administer anti-IgE, which prevents exacerbations, improves symptoms, and reduces the use of inhaled steroids in patients with moderate-to-severe asthma (Corren et al., 2003; Lanier et al., 2003).	Ib	Indirect outcome (anti-IgE)
Patients who need education on asthma and guidance in techniques for self-management	Use of written action plans improves asthma self-management (Wu et al., 2001; Diette et al., 2001; Mahr & Evans, 1993).	II, III	Indirect outcome (education, action plan)
	Allergist care is more likely to lead to provision of a written management plan and objective monitoring of asthma with peak flow meters (Wu et al., 2001; Diette et al., 2001; Mahr & Evans, 1993).	II, III	
	Asthma self-management education improves outcomes in children and adults (Wolf et al., 2003; Gibson et al., 2002). Allergist care is associated with more effective self-management education and knowledge (Wu et al., 2001; Schatz et al., 2005; Engel et al., 1989; Wolle & Cwi, 1995).	Ia, III	
Patients who use excessive amounts of reliever medications	Excessive short-acting beta-agonist use indicates uncontrolled asthma. Allergist care reduces overuse of short-acting beta-agonists (Diette et al., 2001).	II	Direct outcome
Patients with severe asthma	Allergist care reduces cost of care for asthma (Westely et al., 1997; Weinstein et al., 1992; Weinstein et al., 1996; Freund et al., 1989).	III	Direct outcome

TABLE III, E. Asthma Treatment: Prevention of Mortality

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with potentially fatal asthma (prior severe, life-threatening episode; prior intubation)	**Improved Pharmacologic Therapy**		
	Inhaled steroids have been associated with significant reductions in risk for fatal and near-fatal exacerbation of asthma (Suissa et al., 2000).	III	Indirect outcome (inhaled and oral steroids)
	Allergist-immunologists prescribe inhaled steroids more frequently than primary care physicians, and patients seen and managed by allergist-immunologists are more likely to be taking inhaled steroids regularly (Legorretta et al., 1998; Hartert et al., 1996; Blais et al., 2001; Donahue et al., 2000; Schatz et al., 2003).	III	
	Oral steroid use for attacks reduces the risk of fatal asthma (Abramson et al., 2001; Leung, Santiago, & Klaustermeyer, 1983; "CONTROLLED trial," 1956).	Ib, III	
	Patients managed by allergist-immunologists are more likely to appropriately receive oral steroids (Schatz et al., 2003; Engel et al., 1989; Bucknall et al., 1988).	III	
	Immunologic Therapy		
	Allergens can trigger severe and fatal asthma episodes (O'Hollaren et al., 1991).	III	Indirect outcome (avoidance, immunotherapy)
	Allergist-immunologists have expertise in performance and interpretation of skin tests for immediate hypersensitivity, education to encourage aeroallergen avoidance, and provision of inhalant allergen immunotherapy in properly selected patients ("Allergy and immunology core curriculum," 1996).	IV	
	Allergen immunotherapy provides significant clinical benefit ("Allergen immunotherapy,", 2003; Abramson, Puy, & Weiner, 2003), including for *Alternaria* species (Horst et al., 1990), which has been associated with life-threatening asthma (O'Hallaren et al., 1991).	Ia, Ib, III, IV	
	Anti-IgE therapy has been shown to improve outcomes in high-risk patients (Bousquet et al., 2004; Holgate et al., 2001).	Ia, Ib	

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	Objective Monitoring of "Poor Perceivers"		
	A major factor contributing to risk for fatal asthma outcomes is underrecognition of asthma; some asthmatic patients are "poor perceivers" (Kikuchi et al., 1994).	III	Diagnostic
	Allergist-immunologists perform objective measurements of lung function more frequently than other physicians (Janson & Weiss, 2004; Freund et al., 1988).	III	
	Action Plans		
	Action plans can reduce asthma mortality (Abramson et al., 2001).	III	Indirect outcome (action plans)
	Asthma specialists are more likely to provide action plans to their patients (Diette et al., 2001).	III	

TABLE III, F. Asthma Treatment: Adherence

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with asthma in whom adherence problems might be limiting optimal control	Patients with a visit to an allergist-immunologist in the prior year were significantly more likely to have been dispensed an optimally effective number of inhaled steroid canisters (Schatz et al., 2003).	III	Direct outcome
	Specialty care is associated with more refills of anti-inflammatory medications (Stempel, Carlson, & Buchner, 1997).	III	
	Patient compliance with national asthma guidelines was higher in patients of specialists (Meng et al., 1999).	IV	
	Misunderstanding of asthma controller medications, which was associated with decreased adherence, was more likely in patients not treated by specialists (Farber et al., 2003).	III	

TABLE III, G. Occupational Asthma

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with a history suggesting occupational asthma should undergo	History and physical examination are insufficient to confirm occupational asthma, and	III, IV	Diagnostic Indirect outcome

Referral Guideline	Rationale	Evidence Grade	Evidence Type
testing to confirm the diagnosis of asthma and referral to an allergist for evaluation to establish that the asthma is caused by or triggered by agents at the workplace and to initiate appropriate avoidance therapy.	inaccurate conclusions can easily be drawn (Malo et al., 1991; Baur et al., 1998). Allergists can interpret spirometry when performed as a baseline, with response to bronchodilator, serial assessment of spirometry or peak flows, and changes in methacholine response during work periods versus off-work periods ("Allergy and immunology core curriculum," 1996; Moscato et al., 1995; Vandenplas et al., 2001; Chan-Yeung, 1995; Tarlo et al., 1998; Cartier, Pineau, & Malo, 1984; Cockroft & Mink, 1979).		(avoidance)
	Allergists can outline the algorithm for the clinical investigation of suspected occupational asthma and interpret other studies to confirm bronchial hyperresponsiveness, including challenges with methacholine, histamine, cold air, or exercise, yet realize that such study results might be negative if performed when the patient is off work and free of symptoms ("Allergy and immunology core curriculum," 1996; Vandenplas et al., 2001; Cartier, Pineau, & Malo, 1984).	III, IV	
	Allergists can review Material Safety Data Sheets and other specific details of the workplace obtained either through specific questioning, direct observation during an onsite work evaluation, or assistance in obtaining an industrial hygiene survey in an effort to identify exposure to possible causal agents. Allergists can arrange and interpret workplace challenges and be able to provide assistance in referring to centers that can perform specific agent laboratory challenges if indicated ("Allergy and immunology core curriculum," 1996; Vandenplas et al., 2001; Tarlo et al., 1998).	III, IV	
	The importance of identifying the	III, IV	

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	agent responsible for asthma is that continued exposure can lead to worsening asthma and possibly persistent disease, even after exposure ceases. Early accurate diagnosis and removal from further exposure to specific work sensitizers carries the best medical prognosis for those with occupational lung disease (Moscato et al., 1999; Paggiaro, et al., 1987; Gannon et al., 1993; Chan-Yeung, MacLean, & Paggiaro, 1987; Rosenberg et al., 1987; Tarlo et al., 1997; Perfetti et al., 1998).		
Consider referral of a worker with asthma for evaluation of workplace exposures that could worsen or exacerbate the asthma.	Exposure to workplace irritants is a known cause of and known exacerbator of asthma (Tarlo et al., 2000).	III	Indirect outcome (avoidance)

TABLE IV. Conjunctivitis

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with prolonged or recurrent manifestations of allergic conjunctivitis Patients with comorbid conditions (e.g,. asthma, rhinitis, recurrent sinusitis)	Allergy cannot be diagnosed on the basis of history alone (Martin et al., 2003). Diagnosis is derived from a correlation of clinical history and diagnostic tests, with which allergist-immunologists are experienced ("Allergy and immunology core curriculum," 1996). Allergists can help to suspect and diagnose corneal involvement in vernal and atopic keratoconjunctivitis (Bonini et al., 1999; Bonini et al., 2000).	III, IV	Diagnostic
Patients with symptoms interfering with quality of life, ability to function, or both Patients who have found medications to be ineffective or have had adverse	A thorough allergy evaluation will complement the patient history and aid in the development of specific treatment plans, including immunotherapy and environmental controls. These treatments can benefit patients with allergic conjunctivitis in terms of reduced symptoms, medication use, and cost. Allergen immunotherapy can	Ib, III, IV	Indirect outcome (avoidance, immunotherapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
reactions to previously prescribed medications	be highly effective in controlling the symptoms of allergic conjunctivitis (Mimura et al., 2004; Cakmak et al., 2002; "Allergen immunotherapy," 2003). Efficacy parameters include symptom and medication scores, conjunctival challenge, and immunologic cell markers and cytokine profiles. Allergen immunotherapy can provide lasting benefits after immunotherapy is discontinued (Alvarez-Cuesta et al., 1994; Varney et al., 1991; Bachert et al., 2002).		

TABLE V. Cough

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with chronic cough of 3 to 8 weeks or more	Asthma, postnasal drainage, and gastroesophageal reflux disease are the most common causes of cough (Irwin et al., 1998; Kastelik et al., 2005). Spirometry and a chest radiograph have been suggested as the minimum investigations required in the evaluation of chronic cough (Kastelik et al., 2005; Chang & Robertson, 2000; Morice et al., 2004). Allergists have extensive training to evaluate the upper, as well as lower, airways in a patient with chronic cough ("Allergy and immunology core curriculum," 1996).	III, IV	Diagnostic
Patients with coexisting chronic cough and asthma	Cough occurs in all asthmatic subjects (Irwin et al., 1998). However, cough alone is a poor marker of asthma, and asthma might be overdiagnosed in children with cough alone (Chang & Robertson, 2000). The allergist can both provide expert consultation to ensure the diagnosis of asthma is correct and to maximize therapy in the asthmatic subject (see "Asthma" [Tables III, A, through III, G]).	IV	Diagnostic Indirect outcome (avoidance, pharmacologic, and immunologic therapy)
Patients with coexisting chronic cough and rhinitis	Postnasal drip is the single most common cause of chronic cough (Irwin et al., 1998). Allergy skin testing and history-testing correlation can	IV	Diagnostic Indirect outcome (avoidance, pharmacologic, and

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	differentiate allergic from nonallergic rhinitis (see "Rhinitis" [Table XIII, A]). Treatment of rhinitis can improve the cough (Irwin et al., 1998). Treatment of rhinitis by allergists improves patient outcomes (see "Rhinitis" [Table XIII, A]).		immunologic therapy)
Patients with chronic cough and tobacco use or exposure	Tobacco smoke exposure clearly increases cough prevalence and exacerbates any pulmonary condition (Chang & Robertson, 2000). Chronic cough in cigarette smokers is dose related (Morice et al., 2004). Allergists can assist with active steps to minimize or eliminate tobacco smoke exposure ("Allergy and immunology core curriculum," 1996).	IV	Indirect outcome (smoking cessation)

TABLE VI, A. Atopic Dermatitis

Referral Guideline	Rationale	Evidence Grade	Evidence Type
To confirm the diagnosis of atopic dermatitis in a patient with dermatitis	Allergist-immunologists are specifically trained to diagnose atopic dermatitis ("Allergy and immunology core curriculum," 1996). Defining IgE-mediated sensitivity (by means of skin or *in vitro* testing) is useful in the differential diagnosis (Schultz-Larsen & Hanifin, 2002).	IV	Diagnostic
To identify the role of dust mite allergy in patients with atopic dermatitis	Dust mite allergy can trigger atopic dermatitis. In such patients mite avoidance should be helpful (Platts-Mills et al., 1983; Tupker et al., 1996; Huang et al., 2001; Wheatley & Platts-Mills, 2000; Palmer & Friedmann, 2001; Ricci et al., 2000; Gutgesell et al., 2001; Tan et al., 1996; Holm et al., 2001).	Ib, II, III, IV	Diagnostic Indirect outcome (mite avoidance)
To identify the role of food allergy in patients with atopic dermatitis	Approximately 35% of young children with moderate-to-severe atopic dermatitis have food allergy; the association appears less common in adults but is possible (Sampson & Albergo, 1984; Lever et al., 1998; Woodmansee & Christiansen, 2001; Sampson, 2001; Sicherer, Morrow, & Sampsom, 2000; Niggemann et al., 2001; Eigenmann et al., "Prevalence of IgE-mediated," 1998; Reekers et al.,	Ib, III	Diagnostic Indirect outcome (food avoidance)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	1999).		
Patients whose atopic dermatitis responds poorly to treatment	Allergist-immunologists are specifically trained and experienced in managing atopic dermatitis in both children and adults (Leung et al., 1997; Leung et al., 2004; Hoare, Li Wan Po, & Williams, 2000; Van Der Meer et al., 1999; Devillers et al., 2002; Sowden et al., 1991; Salek et al., 1993; Harper et al., 2001).	Ia, Ib, II, IV	Indirect outcome (pharmacologic therapy)

TABLE VI, B. Contact Dermatitis

Referral Guideline	Rationale	Evidence Grade	Evidence Type
To confirm the diagnosis of and identify the cause of contact dermatitis	Allergist-immunologists are specifically trained to diagnose contact dermatitis ("Allergy and immunology core curriculum," 1996). More allergist-immunologists than dermatologists currently perform patch testing (Fonacier et al., 2002; Fonacier & Charlesworth, 2003). If a cause is defined, avoidance therapy can be initiated (Nettis et al., 2003; Mitchell et al., 1982; Lindberg et al., 2004; Li, Sujan, & Wang, 2003; Adams, 1990; Reitschel et al., 2002; Drake et al., 1995; Marks & DeLeo, 1993; Bernstein & Storms, 1995; Marks et al., 1998).	III, IV	Diagnostic Indirect outcome (avoidance)

TABLE VII. Drug Allergy

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with a history of penicillin allergy who have a significant probability of requiring future antibiotic therapy	The vast majority of patients with a history of penicillin allergy can safely use penicillins if an allergy evaluation, often including a penicillin skin test, is performed (Mendelson et al., 1984).	II	Diagnostic Indirect outcome (needed penicillin treatment)
	History alone is inadequate to rule out IgE-mediated allergy to penicillin (Solensky, Earl, & Gruchalla, 2000).	III	
	Penicillin skin testing in advance of need does not cause significant resensitization (Solensky, Earl, & Gruchalla,	II, III	

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	2002; Macy, Mangat, & Burchette, 2003; Nugent et al., 2003; Bittner & Greenberger, 2004).		
	Patients who are shown not to be allergic to penicillin might be able to use more appropriate and potentially less toxic antibiotics, less expensive antibiotics, or both (Macy & Burchette, 2002).	III	
Patients with a history of penicillin allergy in which a penicillin-class antibiotic is the drug of choice	Skin test responses might be negative in such patients, who can then safely receive penicillin.(Macy, Mangat, & Burchette, 2003) Antibiotic desensitization in patients with positive skin test responses renders them transiently tolerant and induces negative skin test responses, indicating blocking of mast cell–IgE activation events (Naclerio, Mizrahi, & Adkinson, 1983; Stark et al., 1987; Solensky, 2004; Borish, Tamir, & Rosenwasser, 1987).	III, IV	Indirect outcome (needed penicillin treatment)
Patients with histories of multiple drug allergy-intolerance	Allergist-immunologists provide a comprehensive plan to evaluate the historical adverse drug reactions and provide suggestions on future therapies to minimize risks ("Allergy and immunology core curriculum," 1996; Demoly et al., 1999; Gruchalla, 2000; Macy, 2004; Vemuir, Tripathi, & Keefe, 2004; Rotskoff et al., 2004).	IV	Diagnostic Indirect outcome (treatment with needed medications)
Patients who might be allergic to protein-based biotherapeutics and require use of these materials	Allergist-immunologists perform skin testing with appropriate concentrations and techniques to determine current sensitivity ("Allergy and immunology core curriculum," 1996; Vemuir, Tripathi, & Keefe, 2004; Rotskoff et al., 2004; Grammer et al., 1988; Dykewicz et al., 1994; Leonard et al., 2002). For example, insulin desensitization allows for	II, III, IV	Diagnostic Indirect outcome (treatment with needed biotherapeutics)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	continued insulin therapy in patients with prior systemic reactions (Grammer, Metzger, & Patterson, 1984; Gossain, Rovner, & Mohan, 1985).		
Patients with histories of adverse reactions to NSAIDs who require aspirin or other NSAIDs	Allergist-immunologists accurately diagnose NSAID sensitivity through challenge testing (Simon, 2003).	IV	Diagnostic
	Allergist-immunologists perform aspirin desensitization in patients with documented aspirin sensitivity who require aspirin for other medical conditions (Solensky, 2004; Simon, 2003).	IV	Indirect outcome (needed NSAID treatment)
	Desensitization in patients with aspirin-exacerbated respiratory disease can improve the control of both upper and lower respiratory tract disease in these patients (Solensky, 2004; Simon, 2003; Stevenson, 2003).	IV	Indirect outcome (improved respiratory symptoms)
Patients who require chemotherapy medication for cancer or other severe conditions and have experienced a prior hypersensitivity reaction to those medications	Desensitization allows for transient tolerance to chemotherapy medications when there is no alternative treatment (Markman et al., 2000; Robinson et al., 2001; Lee, Matulonis, & Castells, 2004).	III	Indirect outcome (needed chemotherapy)
Patients with a history of possible allergic reactions to local anesthetics	Allergist-immunologists are able to perform skin testing and graded challenge to find a safe local anesthetic for future use. Virtually all patients with histories of reactions to local anesthetics can subsequently tolerate the same or an alternate agent (Gall, Kaufmann, & Kalveram, 1996; Schatz, 1984; Macy, Schatz, & Zeiger, 2002).	II, III	Indirect outcome (needed local anesthetic treatment)
HIV-infected patients with a history of adverse reactions to TM-S who need this therapy	Graded TM-S challenges can identify patients who are not currently sensitive to the drug and allow patients with reactions during challenge to	Ib, III	Diagnostic Indirect outcome (needed TM-S therapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	subsequently tolerate the drug and safely continue therapy (Leoung et al., 2001; Bonfanti et al., 2000; Asar, Daneshvar, & Beall, 1994; Nguyen, Weiss, & Wallace, 1995; Belchi-Hernandez & Espinosa-Parra, 1996; Rich et al., 1997; Demoly et al., 1998).		
Patients with a history of reactions to induction agents or to nonpenicillin antibiotics	Allergist-immunologists provide a comprehensive plan to evaluate the historical adverse drug reactions and provide suggestions on future therapies to minimize risks ("Allergy and immunology core curriculum," 1996; Demoly et al., 1999; Gruchalla, 2000; Macy, 2004; Vemuir, Tripathi, & Keefe, 2004; Rotskoff et al., 2004).	IV	Diagnostic Indirect outcome (treatment with needed medications)

HIV = human immunodeficiency virus; NSAID = nonsteroidal anti-inflammatory drug; TM-S = trimethoprim-sulfamethoxazole

TABLE VIII. Food Allergy

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Persons who have limited their diet on the basis of perceived adverse reactions to foods or additives	After allergy evaluation, an estimated one third of perceived adverse reactions to foods and a small fraction of adverse reactions to additives are verified (Young et al., 1994; Bock, 1987; Sloan & Powers, 1986; Altman & Chiaramonte, 1996; Sampson & McCaskill, 1985; Young et al., 1987). Evaluation by an allergist-immunologist is likely to result in an individual's ability to liberalize his or her diet (thereby likely improving nutrition and quality of life).	II, III	Indirect outcome (avoiding unnecessary diet restriction)
Persons with a diagnosed food allergy	The allergist-immunologist can apply and interpret diagnostic tests (skin prick tests, serum food-specific	II, III, IV	Diagnostic Indirect outcome (food avoidance, early

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	IgE assays, and oral food challenges) and advise patients on dietary avoidance and emergency care measures (Bock, 1987; Sampson & McCaskill, 1985; "Allergy and immunology core curriculum," 1996; Sampson, 2001). These are important aspects of care because (1) many allergies are not permanent and should be monitored for resolution (Bock, 1987), and (2) avoidance of allergenic foods and action taken in the event of exposure are difficult to undertake, are prone to errors, and can be dangerous, thus mandating proper education (Sicherer, Forman, & Noone, 2000; Bock, Munoz-Furlong, & Sampson, 2001).		pharmacologic treatment of reaction)
Atopic families with or expecting a newborn who are interested in identifying risks for and preventing allergy	Family history is the strongest predictor of allergy. A sibling born to a family who already has a child with peanut allergy has a risk for that allergy that is more than 10 times greater than that of the general population (Sicherer et al., 2000). Specific guidelines are in place to approach potential allergy in a food allergy–prone child (eg, breast-feeding and avoidance of allergenic foods) (American Academy of Pediatrics, Committee on Nutrition, 2000; Muraro et al., 2004). Meta-analyses of studies shows breast-feeding and avoidance of cow's milk–soy in the first year might reduce the risk for allergic disease (Gdalevich et al., 2001; Osborn & Sinn, 2003). The allergist-immunologist	Ia, II, IV	Diagnostic Indirect outcome (prevention of sensitization)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	can evaluate the risks and explain possible approaches.		
Persons who have experienced allergic symptoms (urticaria, angioedema, itch, wheezing, and gastrointestinal responses) in association with food exposure	The allergist-immunologist can perform diagnostic tests, such as skin tests, serum IgE tests, and oral food challenges to determine the cause of the reaction (Bock, 1987; "Allergy and immunology core curriculum," 1996; Sampson, 2001; Eigenmann & Sampson, 1998).	II, III, IV	Diagnostic Indirect outcome (food avoidance)
Persons who experience an itchy mouth from raw fruits and vegetables	These symptoms are typical of pollen-food allergy syndrome, or oral allergy syndrome, which can sometimes progress to or overlap with more severe allergic reactions (Ortolani et al., 1989; Ortolani et al., 1988; Crespo et al., 2002). The allergist-immunologist evaluates the reactions to determine the cause and to advise which foods to avoid, identify other potential problematic foods, and assess risks for a severe reaction.	II, III	Diagnostic Indirect outcome (food avoidance)
Infants with recalcitrant gastroesophageal reflux or older individuals with recalcitrant reflux symptoms, particularly if they experience dysphagia	Food allergy might be a cause of infantile reflux, and evidence of food responsiveness is high (about 40%) for children in whom symptoms do not respond well to standard therapies (Iacono et al., 1996). Older individuals might have reflux symptoms and possibly dysphagia caused by eosinophilic esophagitis, a disorder that is also commonly food responsive (Orenstein et al., 2000; Spergel et al., 2002).	II, III	Diagnostic Indirect outcome (food avoidance)
Infants with gastrointestinal symptoms, including vomiting, diarrhea (particularly with blood),	There are a group of food-responsive gastrointestinal disorders of infancy (including food protein–	II, III, IV	Diagnostic Indirect outcome (food avoidance)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
poor growth, and/or malabsorption, whose symptoms are otherwise unexplained, not responsive to medical management, and/or possibly food responsive (even if screening allergy test results are negative)	induced enteropathy, enterocolitis, and proctocolitis) that can be diagnosed, treated, and monitored with modalities with which allergist-immunologists are expert, including elimination diets and oral food challenges ("Allergy and immunology core curriculum," 1996; Lake, Whitington, & Hamilton, 1982; Sampson & Anderson, 2000; Sampson, Sicherer, & Birnbaum, 2001; Sicherer, Eigenmann, & Sampson, 1998). Most of the disorders affecting infants cannot be identified with simple screening tests (Lake, Whitington, & Hamilton, 1982; Sampson & Anderson, 2000; Sampson, Sicherer & Birnbaum, 2001; Sicherer, Eigenmann, & Sampson, 1998).		
Persons with known eosinophilic inflammation of the gut	Eosinophilic gastroenteritis, esophagitis, and/or gastroenterocolitis might be food responsive (Orenstein et al., 2000; Spergel et al., 2002). Patients' symptoms could improve after identification and elimination of causal foods (Spergel et al., 2002), modalities for which the allergist-immunologist is expert.	II, III	Diagnostic Indirect outcome (food avoidance)

TABLE IX. Hypersensitivity Pneumonitis (HP)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Early referral of patients with suspected hypersensitivity pneumonia to avoid continued environmental exposure resulting in	Early accurate diagnosis and removal from further exposure to specific sensitizers carries the best medical prognosis for those with HP (Weltermann et al., 1998; Banaszak, Thiede, & Fink, 1970; Kawai, Tamura, & Murao,	III, IV	Diagnostic Indirect outcome (avoidance)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
permanent lung injury	1984; Zacharisen et al., 1998). Allergists are trained and experienced in environmental exposure history, physical examination, and clinical and laboratory diagnosis of HP ("Allergy and immunology core curriculum," 1996).		
Diagnostic consultation in patients found to have NSIP	Histologic diagnosis of HP varies from the acute stage, subacute stage, and chronic form. Findings of NSIP should initiate the diagnostic consideration of HP because avoidance of the offending antigen and pharmacologic therapy might result in resolution of the disease or stop the progression of disease (American Thoracic Society, 2001).	IV	Diagnostic Indirect outcome (avoidance and corticosteroids)
Patients with known HP for management	Allergist-immunologists are specifically trained to evaluate environmental exposures, evaluate immunologic results, and treat and follow HP, including oral corticosteroid treatment ("Allergy and immunology core curriculum," 1996; Tripathi & Grammer, 2001; Bernstein et al., "Machine Operator's lung", 1995; Dykewicz et al.; 1988; Malo & Zeiss, 1982; Vandenplas et al., 1993; Baur, 1995).	III, IV	Indirect outcome (avoidance and corticosteroids)

NSIP = nonspecific interstitial pneumonia

TABLE X. Insect Hypersensitivity

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Consider referral of patients with systemic reactions suspected or possibly caused by insect stings for accurate identification of specific allergen and consideration for venom	Up to 3% of the population is at risk for anaphylaxis to insect stings, with approximately 40 documented deaths annually (Chafee, 1970; Settipane & Boyd, 1970; Antonicelli, Beatrice Bilo, & Bonifazi,	II, III, IV	Diagnostic Indirect outcome (avoidance, early pharmacologic treatment of reaction, immunotherapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
immunotherapy (or whole-body extract in case of fire ant)	2002; Golden, 1989; Charpin, Birnbaum, & Vervloet, 1994; Barnard, 1973; DeShazo, Butcher, & Banks, 1990; Freeman et al., 1992).		
	Patient identification of the specific insect species causing an allergic reaction is frequently incorrect.		
	Allergy testing and history-test correlation can more accurately identify specific insects responsible for an allergic reaction and can be helpful in diagnosis, treatment, and avoidance recommendations (DeShazo, Butcher, & Banks, 1990; Hunt et al., 1976; Rueff et al., 1996; Georgitis & Reisman, 1985; Golden et al., 1997; Golden et al., 2001; Moffitt, Barker, & Stafford, 1997; Oude Elberink & Dubois, 2003; Reisman, 1994; Portnoy et al., 1999; Moffitt et al., 2004).	II, III, IV	
	Skin testing is generally preferred over in vitro testing for the initial evaluation of venom-specific IgE antibodies (Golden, 1989; Charpin, Birnbaum, & Vervloet, 1994; Golden, 2001; Oude, 2003; Portnoy et al., 1999; Moffitt et al., 2004; Valentine, 1993; Valentine, 1984; Schwartz et al., 1981).	II, IIII, IV	
	Venom immunotherapy (or fire ant whole-body extract) greatly reduces the risk of systemic reactions in stinging insect–sensitive patients (Settipane & Boyd, 1970; Antonicelli, Beatrice Bilo, & Bonifazi, 2002; Charpin, Birnbaum, & Vervloet, 1994;	Ib, II, III, IV	

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	Feeman et al., 1992; Oude Elberink & Dubois, 2003; Hunt et al., 1978; Triplett, 1973; Valentine, Schuberth, & Kagey-Sobotka, 1990).		
	Venom immunotherapy can prevent death caused by subsequent stings in hypersensitive patients (Antonicelli, Beatrice Bilo, & Bonifazi, 2002; Charpin, Birnbaum, & Vervloet, 1994; Oude Elberink & Dubois, 2003; Sasvary & Muller, 1994).	III, IV	
Consider referral of patients with systemic reactions suspected or possibly caused by biting insects for accurate identification of specific allergen	Biting insects, such as *Triatoma* species and mosquitoes, have been identified as a cause of systemic reactions (Feingold & Benjamin, 1961; Hoffman, 2003; McCormack et al., 1995; Rohr, Marshall, & Saxon, 1984; Simons & Peng, 2003.)	II, III, IV	Diagnostic Indirect outcome (avoidance, appropriate pharmacologic therapy)
	RASTs and skin tests to *Triatoma* species salivary gland extracts and whole-body extracts of other biting insects have been used to identify antigen-specific IgE in sera of hypersensitive patients (Gauci et al., 1990; Hoffman, 2004; Peng et al., 1998; Peng, Yang, & Simons, 1995; Pinnas, Chen, & Hoffman, 1978; Reunala et al., "Frequent occurrence of IgE", 1994; Reunala et al., "Passive transfer of cutaneous", 1994, Shan et al., 1995; Trudeau et al., 1993; Van Wye et al., 1991).	III, IV	
	Patient education by an allergist-immunologist, including the cause of the allergy, specific avoidance measures, recognition and treatment of anaphylaxis, and management of local	II, III, IV	

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	side effects, might reduce patient anxiety and potentially reduce morbidity from future bites (Feingold & Benjamin, 1961; Hoffman, 2003; McCormack et al., 1995; Rohr, Marshall, & Saxon, 1984; Simons & Peng, 2003).		
Consider referral of patients receiving venom (or fire ant whole-body extract) immunotherapy annually for review of interval history, tolerance of immunotherapy, need for repeat testing, and need for continued therapy	Regular review of interval history, immunotherapy dosing schedule, and adverse events can contribute to reduced complications of treatment (Portnoy et al., 1999; Moffitt et al., 2004).	IV	Indirect outcome (avoidance, early pharmacologic therapy, immunotherapy)
	Regular review might identify new comorbidities or medications that increase the risk of poor outcomes from natural stings or insect immunotherapy reactions (Portnoy et al., 1999; Moffitt et al., 2004; Hepner et al., 1990; Hermann & Ring, 1997; Simon, Potier, & Thebaud, 1996; Toogood, 1988).	II, III, IV	
	Assessment of reactions to interval stings can be used to monitor the effectiveness of immunotherapy and might be cause for consideration of changes in dose and schedule (Portnoy et al., 1999; Moffitt et al., 2004; Golden et al., 1981; Rueff, Wenderoth, & Przybilla, 2001; Tracy et al, 1995; Reisman & Livingston, 1992).	II, III, IV	
	The interval between maintenance dose injections can be increased to 4-week intervals during the first year of immunotherapy and eventually to every 6-12 weeks in some patients (Portnoy et al., 1999; Moffitt et al., 2004; Reisman & Livingston, 1992; Goldberg &	II, III, IV	

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	Confino-Cohen, 2001).		
	Many patients can safely discontinue venom immunotherapy after at least 3-5 years of treatment, although some patients might need to continue immunotherapy indefinitely. An allergist-immunologist with experience in treating patients with insect venom allergy is best suited to facilitate individualized patient decisions (Portnoy et.al., 1999; Moffitt et al., 2004; Golden et al., 1981; Golden, Kwiterovich, & Kagey-Sobotka, 1996; Golden, Kagey-Sobotka, & Lichtenstein, 2000; Golden et al., 1998; "The discontinuation of Hymenoptera," 1998; Hauguaard, Norregard, & Dahl, 1991; Keating et al., 1991; Lerch & Muller, 1998; Light, 2001; Muller, Berchrold, & Helbring, 1991; "The diagnosis and management of anaphylaxis," 1998; Reisman, 1993; Ross, Nelson, & Finegold, "Effectiveness of specific immunotherapy in the treatment of hymenoptera venom," 2000).	II, III, IV	

RAST = radioallergosorbent test

TABLE XI. Occupational Allergic Diseases

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Workers (1) who anticipate being exposed to an agent or agents to which they are at risk of allergy development or (2) who are presently being	Workers with congenital urogenital tract abnormalities, patients with spina bifida, health care workers, and rubber workers have a very	III, IV	Diagnostic Indirect outcome (avoidance)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
exposed to and are at risk for an allergic reaction to an agent, including rhinitis, conjunctivitis, asthma or eczema, should be referred to an allergist-immunologist for assessment to determine whether the worker might be susceptible to rhinitis, asthma, dermatitis, urticaria, or anaphylaxis from the exposure. An example is a worker who will be exposed to latex and has spina bifida, congenital urogenital tract abnormalities, or a worker with a past history suggestive of latex allergy.	high prevalence of latex allergy (Yassin et al., 1992; Liss et al., 1997; Wartenberg & Buckler, 2001; Rueff et al., 2001; Tarlo et al., 2001).		
	Workers with an allergy who might not be able to prevent exposure or are prone to accidental exposure should be educated on self-treatment of asthma, rhinitis, urticaria, eczema, and anaphylaxis and have appropriate medications to use to control symptoms and signs. Specifically, if the patient has a history of anaphylaxis, prescribing and educating the patient on the proper use of an EpiPen or similar device for self-administration of epinephrine might be life saving. Allergist-immunologists are specifically trained to educate patients regarding self-treatment of such reactions (Hamilton & Adkinson, 1998).	III	
Workers in whom the cause of occupationally induced lung disease, including asthma or hypersensitivity pneumonitis, skin disease, or upper respiratory disease, such as rhinitis or conjunctivitis, is unable to be determined on the basis of history alone, or objective evidence is necessary to confirm cause and effect between exposure and disease.	Skin testing and RAST testing often can identify the cause of a hypersensitivity reaction ("Allergy and immunology core curriculum," 1996).	IV	Diagnostic Indirect outcome (avoidance)
	Continued exposure to an allergen might result in progressive lung volume loss, which could be irreversible (Perfetti et al., 1998).	III	
	In most cases avoidance of the identified agent is the optimal treatment for occupational diseases (Vedal et al., 1986).	III	
	Correlation of the history with the results of IgE testing helps prevent inappropriate avoidance, which might be suggested by RASTs alone (Bernstein et al., 1999; Chan-Yeung & Malo, 1995). In cases in which the cause cannot be	III, IV	

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	isolated adequately on the basis of history, skin tests, or RASTs, inhalation challenge, which is the gold standard, can be arranged to provide objective evidence of a hypersensitivity reaction (Vandenplas & Malo, 1997).		
Workers with occupationally induced rhinoconjunctivitis	Workers with rhinoconjunctivitis are at an increased risk of asthma. Early avoidance might decrease the risk of further respiratory disease (Malo et al., 1997). By means of history, skin tests, and/or RASTs and correlating the history and objective findings, the causative agent can often be identified, allowing appropriate avoidance and preventing possible loss of occupation or serious lung disease (Rodier et al., 2003). Prognosis of occupationally induced respiratory disease is dependent on the extent and duration of exposure (Nguyen et al., 2003).	III	Diagnostic Indirect outcome (avoidance)
Referral to an allergist-immunologist for career counseling should be considered for adolescents with allergic disease who might be considering careers with exposure to animals or other allergens.	On the basis of history and relevant studies, allergist-immunologists can assess the future relative risks of such patients in the workplace ("Allergy and immunology core curriculum," 1996; Sjostedt & Willers, 1989). These individuals can then be aware of any degree of increased risk of sensitization and be able to modify career plans with suitable advice.	III, IV	Indirect outcome (avoidance)
Workers in occupations with animal exposure who experience rash, upper respiratory tract symptoms, eye symptoms, or lung symptoms	Upper respiratory and lower respiratory tract, skin, and eye symptoms might be due to allergic sensitization to the animals. Allergy testing can confirm sensitization and lead to appropriate interventions (Sjostedt & Willers, 1989).	III	Diagnostic Indirect outcome (avoidance)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Persons with occupational exposure to food proteins and chronic skin symptoms, respiratory symptoms, or both, attributable to the work environment	Occupational disease might be related to exposure to food proteins, such as wheat (''Baker's'' asthma), or food handling (contact urticaria, contact dermatitis) that is diagnosed through modalities available to the allergist-immunologist ("Allergy and immunology core curriculum," 1996). Avoidance is the treatment of choice (Carmona et al., 1992; Thiel & Ulmer, 1980).	III, IV	Diagnostic Indirect outcome (avoidance)

TABLE XII. Primary Immune Deficiency

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Any of the following warning signs: • 8 or more new infections within 1 year • 2 or more serious sinus infections within 1 year • 2 or more months on antibiotics with little or no effect • 2 or more pneumonias within 1 year • failure of an infant to gain weight or grow normally • recurrent deep skin or organ abscesses • persistent thrush in the mouth or elsewhere on skin after age 1 year • need for	Frequent infection, unusual infections, or unusual complications of usual infections are the most frequent presentation of immune deficiency (Bonilla et al., 2005; Ballow, 2002; Buckley, 2002; "Primary immunodeficiency diseases," 1999; Amaiz-Villena et al., 1995; Champi, 2002; Fleisher, 1996). Advanced diagnostic strategies are necessary to ensure appropriate diagnosis and treatment (Bonilla et al., 2005; Champi, 2002; Fleisher, 1996; Wasserman & Sorensen, 1999). Allergist-immunologists are trained to diagnose and treat primary immunodeficiency ("Allergy and immunology core curriculum," 1996).	III, IV	Diagnostic
	Immunologic therapy improves immunity (Hershfield, 1995; Cunningham-Rundles et al., 2001), reduces infections (Nydahl-Persson, Petterson, & Fasth, 1995; Gallin et al., 2003; Busse, Razvi, & Cunningham-Rundles, 2002), improves organ function (de Gracia et al., 2004), prevents complications (Bonilla et al., 2005), improves quality of life	Ib, II, III, IV	Indirect outcome (immunologic therapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
intravenous antibiotics to clear infections • 2 or more deep-seated infections • a family history of immune deficiency	(Gardulf et al., 2004), and might be curative (Horwitz et al., 2001, Buckley et al., 1999) in patients with primary immune deficiencies.		

TABLE XIII, A. Rhinitis

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with prolonged or severe manifestations of rhinitis with comorbid conditions (eg, asthma or recurrent sinusitis); with symptoms interfering with quality of life, ability to function, or both; or who have found medications to be ineffective or have had adverse reactions to medications (Dykewicz et al., 1998; "Allergen immunotherapy," 2003; Bousquet, van Cauwenberge, & Khaltaev, 2001)	Allergist-immunologist care for rhinitis is associated with improved quality of life, compliance, and satisfaction with care (Demoly et al., 2002; Bagenstose & Bernstein, 1999).	III	Direct outcome
	Allergy cannot be diagnosed on the basis of history alone (Williams et al., 2003). Allergist-immunologists are highly trained to interpret the clinical history and allergy diagnostic test results in both upper and lower airway conditions ("Allergy and immunology core curriculum," 1996).	III, IV	Diagnostic
	Allergist-immunologists have familiarity with the wide variety of both indoor and outdoor aeroallergen exposures that have been shown to affect the upper respiratory tree and have the expertise to provide avoidance education ("Allergy and immunology core curriculum," 1996).	IV	Indirect outcome (avoidance)
	Allergen immunotherapy can be highly effective in controlling the symptoms	Ib, IV	Indirect outcome (immunotherapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	of allergic rhinitis (Bousquet, Lockey, & Malling, 1998). Allergen immunotherapy might provide lasting benefits after immunotherapy is discontinued (Durham et al., 1999).		
Patients with nasal polyps	Allergist-immunologists are specifically trained and experienced in the medical management of nasal polyps, including intranasal steroids, oral steroids, and treatment of complicating sinusitis (Dykewicz et al., 1998; "Allergy and immunology core curriculum," 1996).	IV	Indirect outcome (pharmacologic therapy)
In addition to the above guidelines, consider referral of the child with allergic rhinitis because of the potential preventive role of allergen immunotherapy in progression of allergic disease.	Allergen immunotherapy has been shown to reduce development of new sensitizations and asthma in children with allergic rhinitis compared with children with allergic rhinitis treated with medication alone (Moller et al., 2002).	Ib	Indirect outcome (immunotherapy)

TABLE XIII, B. Sinusitis

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with chronic rhinosinusitis of any type	This set of conditions related to chronic inflammation of the sinus and contiguous nasal mucosa often coexists with allergic rhinitis (Steinke & Borish, 2004). Allergist-immunologist care is associated with improved outcomes (McNally, White, & Kaliner, 1997).	III, IV	Direct outcome
	Allergy immunotherapy is demonstrated to improve outcomes in patients with concomitant allergic rhinitis (Nathan et al., 2004).	III	Indirect outcome (immunotherapy)
Patients with chronic or recurrent	Many patients with this condition have humoral immunodeficiency, cystic fibrosis, fungal sinusitis, or	IV	Diagnostic Indirect outcome (avoidance,

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Infectious rhinosinusitis	granulomatous diseases (Steinke & Borish, 2004). Allergist-immunologists are trained in the evaluation and management of these disorders ("Allergy and immunology core curriculum," 1996).		pharmacologic, and immunologic therapy)
Patients with chronic eosinophilic rhinosinusitis	This is a chronic inflammatory disease with characteristics of allergic inflammation (Steinke & Borish, 2004). It often coexists with aspirin sensitivity, asthma, and sinus-nasal polyposis Borish, 2002; Szczeklik & Stevenson, 2003). Allergist-immunologists are experts in allergic inflammation and can evaluate and treat both environmental allergy and aspirin sensitivity ("Allergy and immunology core curriculum," 1996).	IV	Diagnostic Indirect outcome (avoidance, pharmacologic, and immunologic therapy)
Patients with allergic fungal rhinosinusitis	This is a chronic inflammatory disease with characteristics of IgE and eosinophilic inflammatory response to fungi in sinuses (Schubert, 2004; Schubert, & Goetz, "Evaluation and treatment of allergic fungal sinusitis. I.", 1998). Evaluation involves allergy skin testing and other laboratory testing (Schubert & Goetz, "Evaluation and treatment of allergic fungal sinusitis. II," 1998). Management involves medical management, allergen immunotherapy, and surgery (Schubert & Goetz, "Evaluation and treatment of allergic fungal sinusitis. II," 1998; Mabry et al., 1998). Allergist-immunologists are experts in the evaluation and management of allergic diseases, including allergy immunotherapy ("Allergy and immunology core curriculum," 1996).	III, IV	Diagnostic Indirect outcome (pharmacotherapy, immunotherapy)

TABLE XIV. Urticaria and Angioedema (see also "Anaphylaxis" [Table II]), "Drug Allergy" [Table VII], and "Food Allergy" [Table VIII])

Referral Guideline	Rationale	Evidence Grade	Evidence Type
Patients with acute urticaria or angioedema without an obvious or previously defined trigger	After a severe allergic reaction without a known cause, a trigger should be identified, if at all possible ("The diagnosis and management of urticaria," 2000). An allergist-immunologist is the most appropriate medical professional to perform this evaluation ("Allergy and immunology core curriculum," 1996), which might include a detailed history, physical examination, skin testing, *in vitro* testing, and challenges when indicated.	IV	Diagnostic
	Future avoidance of the identified triggers should prevent subsequent anaphylactic episodes.		Indirect outcome (avoidance)
Patients with acute urticaria or angioedema caused by a presumed food or drug with need for diagnostic confirmation or assistance with avoidance procedures	See "Food Allergy" (Table VIII) and "Drug Allergy" (Table VII)		Diagnostic Indirect outcome (avoidance)
Patients with chronic urticaria or angioedema (ie, those with lesions recurring persistently over a period of 6 weeks or more)	Allergists and dermatologists have more expertise in caring for patients with urticaria than other specialists (Henderson, Fleischer, & Feldman, 2000). Chronic urticaria often has an autoimmune pathogenesis (Kaplan, 2004). Consultation with an allergist-immunologist would include (1) reviewing possible causative factors (medications, supplements, dietary factors, animal exposures, and physical factors), (2) possible skin testing, (3) possible physical challenges, (4)	Ib, III, IV	Diagnostic Indirect outcome (avoidance, pharmacotherapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
	recommended changes in ingestants or contactants, and (5) optimal pharmacotherapy ("The diagnosis and management of urticaria," 2000; "Allergy and immunology core curriculum," 1996; Henderson, Fleischer, & Feldman, 2000; Kaplan, 2004; Dibbern & Dreskin, 2004; Finn et al., 1999; Kalivas et al., 1990; Greene, Reed, & Schroeter, 1985). Allergy-immunology specialists are also knowledgeable of the minimal benefit of multiple laboratory tests in urticaria with an otherwise normal examination ("The diagnosis and management of urticaria," 2000; "Allergy and immunology core curriculum," 1996; Henderson, Fleischer, & Feldman, 2000).		
Patients who might have urticarial vasculitis or urticaria with systemic disease (vasculidities, connective tissue disease, rarely malignancies): a. Lesions last more than 24 hours; leave ecchymotic, purpuric, or hyperpigmented residua on or under the skin; or are associated with pain or burning b. Patients who have typical urticaria-angioedema but have signs and	Allergist-immunologist training and expertise should allow appropriate differential diagnosis, determination of the need for biopsy, elimination of a specific inciting agent, and optimal pharmacotherapy ("Allergy and immunology core curriculum," 1996; Dibbern & Dreskin, 2004; Davis & Brewer, 2004; Mehregan, Hall, & Gibson, 1992).	III, IV	Diagnostic Indirect outcome (avoidance, pharmacotherapy)

Referral Guideline	Rationale	Evidence Grade	Evidence Type
symptoms suggestive of systemic illness C. Patients whose symptom control requires regular steroid use			
Patients with chronically recurring angioedema without urticaria	Such patients might have hereditary or acquired angioedema, paraproteinemia, or B-cell malignancies. Allergist-immunologist expertise should allow optimal differential diagnosis, determination of the need for hematology-oncology evaluation, and pharmacologic therapy of hereditary or acquired angioedema caused by C1 esterase inhibitor deficiency (Cicardi et al., 2003; Agostoni et al., 2004; Gelfand et al., 1976).	Ib, III, IV	Diagnostic Indirect outcome (pharmacotherapy)
Patients with suspected or proved cutaneous or systemic mastocytosis	Allergist-immunologists are trained to diagnose and treat this disease ("Allergy and immunology core curriculum," 1996; Brockow, 2004; Akin & Metcalf, 2004; Valent et al., 2004).	IV	Diagnostic Indirect outcome (pharmacotherapy)

Definitions:

The evidence cited is graded according to the following system:

- Ia. Meta-analysis of randomized controlled trials
- Ib. Randomized controlled trial
- II. Nonrandomized, controlled intervention study
- III. Observational cohort or case-control study
- IV. Review article, expert opinion

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

REFERENCES SUPPORTING THE RECOMMENDATIONS

References open in a new window

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence supporting each referral guideline is specifically stated and graded (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

For many patients with asthma and allergic diseases, working with an allergist-immunologist can assist them in managing their disease and preventing morbidity and mortality.

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The consultation and referral guidelines were based on evidence that allergist-immunologist care improves patient outcomes. This was either direct evidence that outcomes improved with allergist-immunologist care or evidence that diagnostic or therapeutic interventions performed by allergist-immunologists improved outcomes. Because there has been a paucity of controlled intervention trials addressing this issue, the evidence is often observational. Some of the rationale statements are only supported by consensus or expert opinion. The Academy believes that trying to provide a rationale for each guideline and citing the best available evidence is a step forward in creating rational, useful, and evidence-based guidelines for consultation and referral.
- Although some patients will require ongoing allergist-immunologist management, others might require just a single or a limited number of consultations. Still others might benefit from coordinated primary care and allergist-immunologist follow-up (co-management).

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The American Academy of Allergy, Asthma, and Immunology has promoted the availability of these guidelines to primary care providers through their professional

associations and journals. In addition, they have made these guidelines available to managed care organizations through America's Health Insurance Plans.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

American Academy of Allergy, Asthma & Immunology. Consultation and referral guidelines citing the evidence: how the allergist-immunologist can help. J Allergy Clin Immunol 2006 Feb;117(2 Suppl Consultation):S495-523. [371 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Feb

GUIDELINE DEVELOPER(S)

American Academy of Allergy, Asthma and Immunology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Academy of Allergy, Asthma and Immunology

GUIDELINE COMMITTEE

Task Force of the American Academy of Allergy Asthma and Immunology

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Editors: Donald Leung, MD, PhD, FAAAAI; Michael Schatz, MD, MS, FAAAAI

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

- M. Schatz has received research grants from GlaxoSmithKline and Sanofi-Aventis and has received honoraria for lecturing on the subjects of asthma control, asthma and pregnancy, and the burden of rhinitis from AstraZeneca, Genentech, GlaxoSmithKline, and Merck.
- D. Leung—none disclosed

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Journal of Allergy and Clinical Immunology Web site:

- HTML format
- Portable Document Format (PDF)

Print copies: Available from the American Academy of Allergy, Asthma & Immunology, 555 East Wells Street, Suite 1100, Milwaukee, WI 53202-3823; Phone: (414) 272-6071

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

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